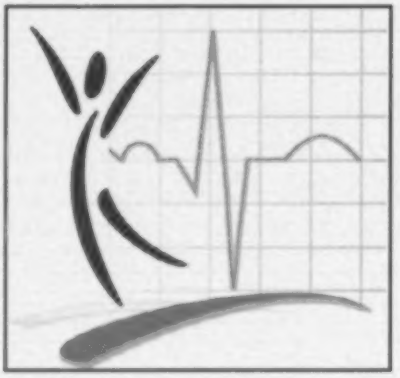
Catalogue no.82-624-X
ISSN 1925-6493

Health at a Glance

# Deaths involving sepsis in Canada



by Tanya Navaneelan, Sarah Alam, Paul A. Peters, and Owen Phillips

Release date: January 21, 2016

Statistics Canada Statistique Canada

Canada

## How to obtain more information

For information about this product or the wide range of services and data available from Statistics Canada, visit our website, www.statcan.gc.ca.

You can also contact us by

**email at** STATCAN.infostats-infostats.STATCAN@canada.ca

**telephone,** from Monday to Friday, 8:30 a.m. to 4:30 p.m., at the following toll-free numbers:

- Statistical Information Service 1-800-263-1136
- National telecommunications device for the hearing impaired 1-800-363-7629
- Fax line 1-877-287-4369

**Depository Services Program**

- Inquiries line 1-800-635-7943
- Fax line 1-800-565-7757

## Standards of service to the public

Statistics Canada is committed to serving its clients in a prompt, reliable and courteous manner. To this end, Statistics Canada has developed standards of service that its employees observe. To obtain a copy of these service standards, please contact Statistics Canada toll-free at 1-800-263-1136. The service standards are also published on www.statcan.gc.ca under "Contact us" > "Standards of service to the public."

## Note of appreciation

Canada owes the success of its statistical system to a long-standing partnership between Statistics Canada, the citizens of Canada, its businesses, governments and other institutions. Accurate and timely statistical information could not be produced without their continued co-operation and goodwill.

## Standard table symbols

The following symbols are used in Statistics Canada publications:

. not available for any reference period
.. not available for a specific reference period
... not applicable
0 true zero or a value rounded to zero
$0^s$ value rounded to 0 (zero) where there is a meaningful distinction between true zero and the value that was rounded
$^p$ preliminary
$^r$ revised
x suppressed to meet the confidentiality requirements of the *Statistics Act*
$^E$ use with caution
F too unreliable to be published
* significantly different from reference category ($p < 0.05$)

Published by authority of the Minister responsible for Statistics Canada

© Minister of Industry, 2016

All rights reserved. Use of this publication is governed by the Statistics Canada Open Licence Agreement.

**An** HTML version **is also available.**

*Cette publication est aussi disponible en français.*

Health at a Glance

# Deaths involving sepsis in Canada

by Tanya Navaneelan, Sarah Alam, Paul A. Peters, and Owen Phillips

## Highlights

- In 2011, one in 18 deaths in Canada involved sepsis, a serious medical condition caused by an overwhelming immune response to an infection.
- Deaths involving sepsis increased significantly between 2000 and 2007 and then remained stable between 2007 and 2011.
- Deaths involving sepsis were higher among males than females, although between 2007 and 2011 the difference between the sexes narrowed.
- Sepsis contributed to more than half of all deaths from infectious diseases in Canada during the 2009–2011 time period.

## Introduction

Sepsis is a serious medical condition caused by an overwhelming immune response to an infection. The immune system sets off a series of reactions in the body including widespread inflammation, swelling and blood clotting.[1,2] This results in impaired blood flow, which damages the body's organs by depriving them of nutrients and oxygen. If not treated quickly, sepsis can lead to multiple organ failure and death. It is estimated that 30% to 50% of people who develop sepsis die from it.[3,4] Sepsis also has an economic burden by extending a patient's stay in the hospital[4] and significantly increasing the cost of treatment.[5]

Sepsis was the 12th leading cause of death in Canada in 2011, up from 15th place in 2000.[6,7] Previous research shows that elderly people, males, and non-Caucasians have an increased risk of developing sepsis. People who develop sepsis often have other, pre-existing, conditions. The most common are human immunodeficiency virus (HIV), cancer, diabetes, cirrhosis, alcohol dependence, and bedsores.[8,9]

This article provides the first Canadian estimates of sepsis-associated deaths; that is deaths where sepsis was either an underlying or contributing cause of death. Previous national estimates of sepsis deaths using administrative data sources have only included deaths where sepsis was the underlying cause of death.

## Underlying and contributing causes of death

The Vital Statistics Program at Statistics Canada collects data on deaths through its Canadian Vital Statistics – Deaths Database. Mortality rates are most often estimated using the underlying cause of death as reported on the death certificate. The underlying cause of death is defined as the disease or injury that initiated the series of events that led to death.[10]

However, many deaths have multiple causes. That is, they are the result of not only the underlying cause but also other conditions. These other conditions are contributing causes of death – diseases or injuries which played a part in the death but were not reported as the underlying cause of death. For example, HIV may lead to a suppressed immune system which can lead to infection, ultimately causing sepsis. In this case, HIV may be reported as the underlying cause of death on the death certificate, while sepsis, the specific infection and the suppressed immune system may be reported as contributing causes.

Between 2000 and 2010, only 18% of all deaths in Canada had just an underlying cause reported on the death certificate. On the other hand, 25% of deaths had one reported contributing cause in addition to the underlying cause, 23% had two contributing causes, 16% had three contributing causes, 9% had four contributing causes and 9% had five or more contributing causes.[11]

Only including the underlying causes of death does not allow for a full picture of all factors playing a role in the death. This is particularly true of sepsis for two reasons. First, sepsis is known to be a greater risk for the elderly and for other people with multiple chronic conditions that can make them more likely to get an infection. For these people, sepsis may be a condition that contributed to their death but it may not be listed as the underlying cause of death on the death certificate. Second, many cases of sepsis result from infections acquired in healthcare facilities. In these cases, the original reason for hospitalization, rather than sepsis, is often reported as the underlying cause of death on the death certificate.[8]

Until recently, national multiple-causes-of-death data have only been available for limited use. However, the Vital Statistics - Deaths Database now includes multiple-causes-of-death data for all years starting in 2000.[12,13]

Data presented in this article come from the Canadian Vital Statistics – Deaths Database (CVS:D) and are analysed over time and by sex, age, and underlying cause of death. Data from the years 2000 to 2011 are used when discussing changes over time. Three years of data (2009, 2010 and 2011) are combined when discussing differences by age or underlying cause of death to reduce the random variation that can occur with small numbers.

## One in 18 deaths in Canada involve sepsis

In 2011, there were 2,515 deaths where sepsis was reported as the underlying cause.[14] In addition, there were 10,985 deaths where sepsis was reported as a contributing cause [15]. This means that about one in 18 Canadian deaths involved sepsis that year (an **age-standardized rate** of 27.2 deaths per 100,000 people). This is similar to the level of sepsis-associated deaths found in England and the United States.[8,16]

## Sepsis as a contributing cause of death increased between 2000 and 2007

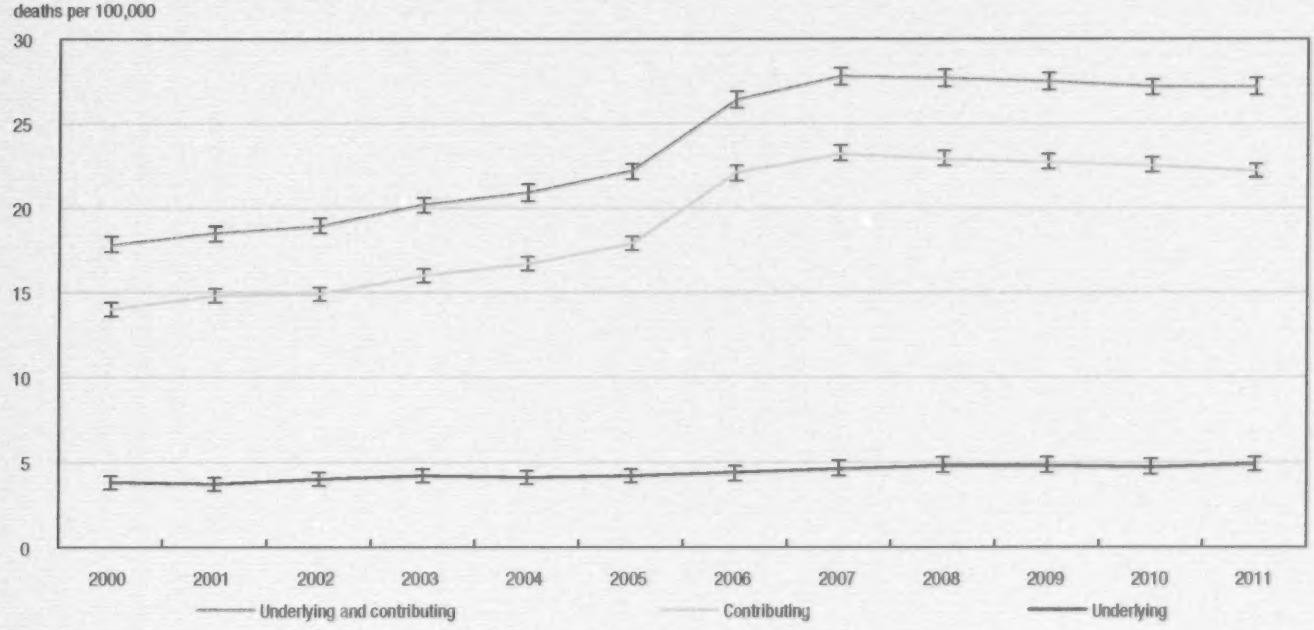
In the early 2000s, the rate of sepsis-associated death (both underlying and contributing) increased significantly (Chart 1). Between 2000 and 2004, the sepsis-associated death rate increased by 4.1% annually.[17,18] The rise was even greater between 2004 and 2007 when there was an increase of 10.6% annually. However, there was no significant change between 2007 and 2011.

The increase in sepsis-associated deaths between 2000 and 2007 was mostly driven by increases in the recording of sepsis as a contributing cause of death. During this time period, the increase in the mortality rate when sepsis was a contributing cause of death (8.5%) was almost three times higher than when it was reported as the underlying cause (2.9%). While this increase in sepsis-associated mortality may reflect an actual increase in deaths involving sepsis, it may also be influenced by other factors including: changes in diagnosis methods and definitions, an increased awareness of sepsis by healthcare professionals, or changes in how deaths are classified.[19,20]

## Males have a higher risk of sepsis-associated death than females

Males had a significantly higher age-standardized rate of sepsis-associated deaths, at 31.7 deaths per 100,000, compared with females (23.8 deaths per 100,000) in 2011. This trend, of higher sepsis-associated deaths in males, was present in all years between 2000 and 2011 (Chart 2).

**Chart 1**
**Sepsis-associated mortality, by type of cause of death, age-standardized rates, Canada, 2000 to 2011**




**Note:** The vertical lines overlaid on the trend lines in this chart indicate the 95% confidence intervals. Confidence intervals indicate the degree of variability in the estimate and enable more valid comparisons of differences between estimates.
**Source:** Statistics Canada, Vital Statistics – Death Database.

One possible reason why males are more likely to have sepsis involved in their death is that they may be more likely than females to develop sepsis in the first place.[16,21] This difference may be related to hormonal and genetic differences between males and females or differences in the presence of other health conditions.[22,23]

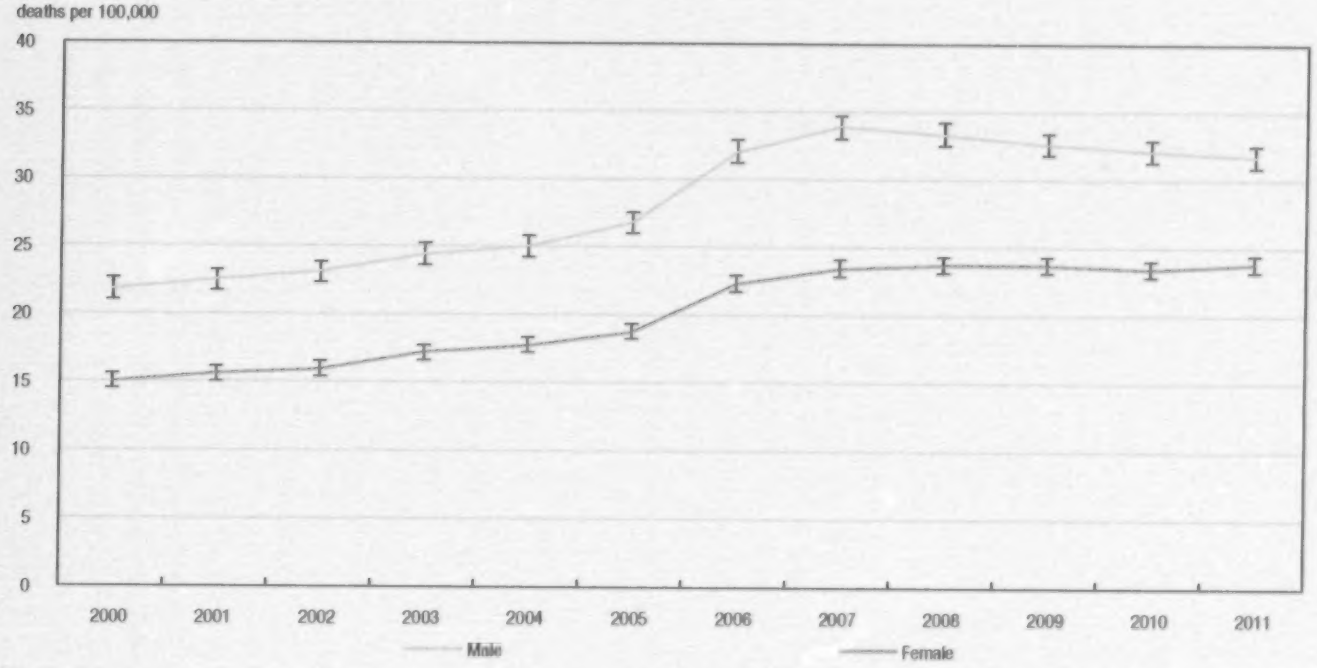
Between 2000 and 2007, sepsis-associated deaths increased significantly for males and females separately, with males having a higher rate of sepsis-associated deaths than females for all years (Chart 2). Since 2007, however, the gap between the sexes has started to close. Between 2007 and 2011, the sepsis-associated mortality rate among males decreased significantly, declining by 1.7% per year, while there was no significant change in the death rate for females during these years. As a result, the difference in the rates between males and females fell from a gap of 10.5 deaths per 100,000 in 2007, to 7.9 per 100,000 in 2011.

## Sepsis-associated deaths increase with age

During the time period 2009–2011, the rate of sepsis-associated deaths increased by age among those 5 and older (Table 1). Deaths involving sepsis were highest among the oldest age group (85 and older) at 587.8 deaths per 100,000 and lowest between ages 5 and 19 (ranging from 0.7 to 0.8 deaths per 100,000). Infants under the age of 1 had a death rate of 33.0 deaths per 100,000, higher than the rates for those aged 1 to 59 years. The pattern of sepsis-associated deaths parallels that of deaths from all causes in Canada, where deaths are highest among the elderly and relatively high in those under the age of one.[24]

Sepsis contributed to deaths in every age group, from newborn babies to the elderly. Among those who died by age 30, sepsis contributed to a relatively similar percentage of mortality, varying between 4.0% and 6.2% of all deaths. (Table 1). However among children (those who died before the age of 15) sepsis contributed to a greater percentage of mortality, varying between 6.7% and 8.2% of all deaths. Adolescents and young adults (ages 15 to -29) were the least likely to have sepsis contribute to their deaths, with 2.0% to 3.3% of all deaths involving sepsis. While children were more likely to have sepsis contribute to their death than adults, older people experienced higher overall mortality than young people, resulting in higher rates of sepsis-associated mortality.

**Chart 2**
**Sepsis-associated mortality, age-standardized rates, by sex, Canada, 2000 to 2011**




**Note:** The vertical lines overlaid on the trend lines in this chart indicate the 95% confidence intervals. Confidence intervals indicate he degree of variability in the estimate and enable more valid comparisons of differences between estimates.
**Source:** Statistics Canada, Vital Statistics – Death Database.

**Table 1**
**Age-specific sepsis-associated mortality rates, Canada, 2009 to 2011**

| | Sepsis-associated mortality | |
|---|---|---|
| Age group | Rate per 100,000 people | % of all deaths |
| All ages | 38.4 | 5.5 |
| Under 1 | 33.0 | 6.7 |
| 1 to 4 | 1.2 | 6.9 |
| 5 to 9 | 0.7 | 8.2 |
| 10 to 14 | 0.8 | 6.7 |
| 15 to 19 | 0.8 | 2.2 |
| 20 to 24 | 1.1 | 2.0 |
| 25 to 29 | 1.7 | 3.3 |
| 30 to 34 | 2.5 | 4.0 |
| 35 to 39 | 4.4 | 5.3 |
| 40 to 44 | 6.0 | 4.8 |
| 45 to 49 | 10.1 | 5.1 |
| 50 to 54 | 17.0 | 5.3 |
| 55 to 59 | 27.3 | 5.5 |
| 60 to 64 | 45.4 | 5.9 |
| 65 to 69 | 72.4 | 6.0 |
| 70 to 74 | 117.7 | 6.1 |
| 75 to 79 | 199.2 | 6.2 |
| 80 to 84 | 323.0 | 5.9 |
| 85 and over | 587.8 | 4.7 |

**Note:** The counts used to create this table have been rounded to a neighbouring multiple of 5 to meet the confidentiality requirements of the *Statistics Act*.
**Source:** Statistics Canada, Vital Statistics – Death Database.

## Sepsis contributes to more than one-half of all deaths from infectious disease

About 5.5% of all deaths in Canada during 2009–2011 were sepsis-associated.[15] Of the underlying causes of death that involved sepsis the most common was diseases of the skin and tissue under the skin (subcutaneous tissue) (61.8%), followed by infectious diseases (53.4%) (see Appendix A).[25,26] Sepsis was also involved in over 10.0% of all deaths from diseases of the: digestive system, musculoskeletal system, and urinary system or genital organs.[27]

Deaths from infectious diseases provide a good example of how sepsis can be both an underlying and contributing cause of death. During 2009–2011, 53.4% of all infectious disease deaths involved sepsis (Table 2). In 82.2% of those deaths, sepsis was the underlying cause of death; while in the other 17.8%, sepsis was a contributing cause of death.

Of the 17.8% of infectious disease deaths where sepsis was a contributing cause there were a number of underlying causes of death. For example, sepsis was involved in almost a quarter of all deaths from bacterial infections of the intestines[20] (e.g., *e. coli* and *c. difficile*); and over 10.0% of all deaths from: tuberculosis, viral infections involving skin lesions[21] (e.g., chickenpox, herpes zoster), HIV and viral hepatitis.

**Table 2**
**Sepsis-associated mortality, by type of infectious disease death, Canada, 2009 to 2011**

| | Sepsis-associated mortality |
|---|---|
| Underlying cause of death | % of all deaths |
| Infectious and parasitic diseases | 53.4 |
| Sepsis | 100.0 |
| Intestinal bacterial infections | 23.3 |
| Tuberculosis | 15.0 |
| Viral infections involving skin lesions | 12.2 |
| HIV | 11.3 |
| Viral hepatitis | 10.8 |
| Other underlying cause | 7.7 |

**Note:** The counts used to create this table have been rounded to a neighbouring multiple of 5 to meet the confidentiality requirements of the *Statistics Act*.
**Source:** Statistics Canada, Vital Statistics – Death Database.

## Conclusion

Of all of the Canadians who died in 2011, sepsis played a role in the death of one in 18. Sepsis was more likely to be reported as a contributing cause rather than the underlying cause of death itself. Including both underlying and contributing causes of death when estimating sepsis-associated deaths, allows for a more complete picture of how sepsis plays a role in overall mortality in Canada. It also means that sepsis-associated deaths can be examined using data from the Vital Statistics Program, providing an alternative to special clinical studies and hospitalization-based analyses.

As the Canadian population ages, sepsis is expected to continue to be a major contributor to mortality and an important health care issue.

Owen Phillips is an analyst with the Health Statistics Division. Tanya Navaneelan and Sarah Alam were with the Health Statistics Division and Paul Peters was with the Health Analysis Division.

## Data source, method and definitions

### Data source

The statistics presented in this article are derived from the multiple-causes-of-death data, produced as part of the Canadian Vital Statistics – Death Database (CVS:D) at Statistics Canada.[11] This dataset includes the underlying and contributing causes of death for deaths that occurred since 2000. Further information on the recording and coding of contributing cause of death information from the death certificate is available in the Vital Statistics User Guide.[11] The CVS:D includes demographic and cause of death information for all deaths from all provincial and territorial vital statistics registries in Canada. Prior to 2010, some data were collected on Canadian residents who died in some American states; these deaths were excluded from this analysis. Starting with the 2010 reference year, data on Canadian residents who died in American states are no longer collected.

### Method

Trends in age-standardized incidence and death rates over time were determined using the Joinpoint Regression Program (v.4.0.4) distributed by the SEER (Surveillance Epidemiology and End Results) program.[10] All trend analyses were performed using age-standardized rates.

To allow for more valid comparisons over time and between populations, age-standardized rates are used to control for differences in population age-structure. The age-standardized rate is the rate that would occur if the population of interest had the same age-structure as the standard population. The standard population used in this article is the July 1, 1991 Canadian population.

Age-standardized rates are used throughout this paper except when rates are given for a specific age group. Rates for individual age groups are called age-specific rates and have not been age-standardized.

### Definitions

Death data were classified according to the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10).[10] There are no codes that directly identify sepsis in the ICD-10. Following previous research into sepsis deaths that used administrative databases, this study used ICD codes for septicaemia as a proxy for sepsis.[8, 15, 21] As there is no standardized coding for sepsis the definition used in this article may not match that used in other studies.

Sepsis was defined by the following codes:

| ICD-10 Chapter | ICD-10 codes |
|---|---|
| Infectious and parasitic diseases | A02.1, A20.2, A20.7, A31.7, A22.7, A26.7, A32.7, A39.2, A39.4, A40, A41, A42.7 |
| Pregnancy, childbirth and the puerperium | O85 |
| Conditions originating in the perinatal period | P36, P37.2 |
| Symptoms, signs and abnormal clinical and laboratory findings | R57.8 |

The underlying cause of death was defined as the cause of death reported on the lowest line of Part I (Disease or condition directly leading to death) of the death certificate. Contributing causes were defined as any causes listed on the other lines of Part I and any causes listed in Part II (other significant conditions contributing to the death).

### Limitations

Multiple-cause-of-death data was not available for parts of the years 2000 to 2002 for Saskatchewan and Yukon. While the total proportion of missing data was small (2.8% of all deaths between 2000 and 2010),[11] an analysis of the data found that the frequency of missing data was not evenly distributed within demographic variables. Therefore there is a potential for bias.

This study relies on the accuracy of the information reported on the death certificate. Unlike leading causes of death, data on contributing causes of death are subjectively documented and may be dependent upon the knowledge, expertise and available time of the person filling out the death certificate.[19]

As there are no codes for sepsis in the ICD-10 this study used septicaemia codes as a proxy for sepsis. While this approach has been validated for ICD-9 and applied to ICD-10 in other studies, it has not yet been validated for ICD-10.[4,16,21] This may have led to misclassification and a possible underestimation of the rate of sepsis-associated death.[8]

## References and notes


1 American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference. 1992. "Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis." *Critical Care Medicine*. Vol. 20, p. 864-874. http://www.ncbi.nlm.nih.gov/pubmed/1597042.

2 Levy M., M. Fink, J. Marshall, et al. 2003. "2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference." *Intensive Care Medicine*. Vol. 91, p. 530-538.

3 Martin, C., F. Priestap, and H. Fisher. 2009. "A prospective, observational registry of patients with severe sepsis: The Canadian Sepsis Treatment and Response Registry." *Critical Care Medicine*, Vol. 37, no. 1, p. 81-88. http://journals.lww.com/ccmjournal/Abstract/2009/01000/A_prospective,_observational_registry_of_patients.12.aspx.

4 Canadian Institute for Health Information (CIHI). 2009. *In Focus: A National Look at Sepsis*. Ottawa, ON. https://secure.cihi.ca/free_products/HSMR_Sepsis2009_e.pdf.

5 Edbrooke, D., C. Hibbert, J. Kingsley, S. Smith, N. Bright, and J., Quinn. 1999. "The patient related costs of care for sepsis patients in a UK adult general intensive care unit." *Critical Care Medicine*. Vol. 27, no. 9, p. 1760-1767. http://journals.lww.com/ccmjournal/Abstract/1999/09000/The_patient_related_costs_of_care_for_sepsis.10.aspx.

6 Statistics Canada. CANSIM Table 102-0561 - *Leading causes of death, total population, by age group and sex*. CANSIM (database). http://www5.statcan.gc.ca/cansim/a26?lang=eng&retrLang=eng&id=1020561&&pattern=&stByVal=1&p1=1&p2=-1&tabMode=dataTable&csid=.

7 In the leading cause of death rankings, sepsis is defined slightly differently than in this article. The difference is approximately 60 deaths annually.

8 Melamed, A. and F. Sorvillo. 2009. "The burden of sepsis-associated mortality in the United States from 1999 to 2005: an analysis of multiple-cause-of-death data." *Critical Care*. Vol. 13, no. 1. http://www.ccforum.com/content/13/1/R28.

9 Angus, D., W. Linde-Zwirble, J. Lidicker, G. Clermont, J. Carcillo and M. Pinsky. 2001. "Epidemiology of severe sepsis in the United States: Analysis of incidence, outcome, and associated costs of care." *Critical Care Medicine*. Vol. 29, no. 7, p. 1303-1310. http://journals.lww.com/ccmjournal/pages/results.aspx?txt=%5b%7b%22Operator%22%3a%22and%22%2c%22FieldP%22%3a%22Title%22%2c%22Key%22%3a%22Epidemiology+of+severe+sepsis+in+the+United+States%22%7d%5d.

10 World Health Organization. 1992. *ICD-10: International Statistical Classification of Diseases and Related Health Problems*, Vol. 1. Geneva: World Health Organization.

11 Statistics Canada. "*Canadian Vital Statistics Program – User Guide*". Available by request.

12 Wilkins, K., M. Wysocki, C. Morin, and P. Wood. 1997. "Multiple causes of death." *Health Reports*. Vol. 9, no. 2, p. 19-29. http://www.statcan.gc.ca/pub/82-003-x/1997002/article/3235-eng.pdf.

13 Park, J., and P. Peters. 2014. "Mortality from diabetes mellitus, 2004 to 2008: A multiple-cause-of-death analysis." *Health Reports*. Vol. 25, no. 3, p. 12-16. http://www.statcan.gc.ca/pub/82-003-x/2014003/article/11909-eng.htm.

14 The data used to calculate underlying cause deaths are based on the underlying cause as reported in the multiple-cause data. Deaths from sepsis are defined using the definition provided in the 'Data source, methods and definitions' box. Due to differences in data sources and definitions, the numbers cited here may not exactly match other national mortality estimates for sepsis.

15 Counts, percentages (except annual percent changes) and age-standardized rates reported in this article have been rounded to a neighbouring multiple of 5 to meet the confidentiality requirements of the *Statistics Act*.

16 McPherson, D., C. Griffiths, M. Williams, A. Baker, E. Kleduwski, B. Jacobson, et al. 2013. "Sepsis-associated mortality in England: An analysis of multiple cause of death data from 2001 to 2010." *BMJ Open*. Vol. 3, no. 8, p. 1-7. http://bmjopen.bmj.com/content/3/8/e002986.full?ad=b7692f1f-dcb2-4894-a25d-c31694124f5a.

17 All trend analysis was performed using age-standardized mortality rates.

18 All annual percent changes (APCs) cited in this article are significant at the $p < 0.05$ level.

19 Messite, J., and S. Stellman. 1996. "Accuracy of death certificate completion: The need for formalized physician training." *The Journal of the American Medical Association*. Vol. 275, no. 10, p. 794-796. http://jama.jamanetwork.com/article.aspx?articleid=398165&resultClick=3.

20 Jordan, J., and M. Ross. 1991. "Errors in death certificate completion in a teaching hospital." *Clinical and Investigative Medicine*. Vol. 16, no. 4, p. 249-255. http://www.ecsdweb.org/publication/1409103/Errors_in_death_certificate_completion_in_a_teaching_hospital.

21 Martin, G., D. Mannino, S. Eaton and M. Moss. 2003. "The epidemiology of sepsis in the United States from 1979 through 2000." *New England Journal of Medicine*. Vol. 348, no. 16, p. 1546-1554. http://www.nejm.org/doi/full/10.1056/NEJMoa022139.

22 Esper, A., M. Moss, C. Lewish, R. Nisbet, D. Mannino and G. Martin. 2006. "The role of infection and comorbidity: Factors that influence disparities in sepsis." *Critical Care Medicine*. Vol. 34, no. 10, p. 2576-2582. http://journals.lww.com/ccmjournal/Abstract/2006/10000/The_role_of_infection_and_comorbidity__Factors.10.aspx.

23 Hubacek, J., F. Stuber, D. Frohlich, et al. 2001. "Gene variants in the bactericidal/permeability increasing protein and lipopolysaccharide binding protein in sepsis patients: Gender-specific genetic predisposition to sepsis." *Critical Care Medicine*. Vol. 29, no. 3, p. 557-561. http://journals.lww.com/ccmjournal/pages/results.aspx?txt=%5b%7b%22Operator%22%3a%22and%22%2c%22FieldP%22%3a%22Title%22%2c%22Key%22%3a%22gene%22%7d%2c%7b%22Operator%22%3a%22and%22%2c%22FieldP%22%3a%22Author%22%2c%22Key%22%3a%22hubacek%22%7d%5d.

24 Statistics Canada. CANSIM Table 102-0504 – *Deaths and mortality rates, by age group and sex, Canada, provinces and territories, annual*. CANSIM (database). http://www5.statcan.gc.ca/cansim/a26?lang=eng&retrLang=eng&id=1020504&pattern=&stByVal=1&p1=1&p2=-1&tabMode=dataTable&csid=.

25 Includes parasitic diseases.

26 Deaths from influenza are classified under diseases of the respiratory system. See Appendix A for more information on sepsis and this cause of death.

27 Diseases of the urinary system and genital organs are also known as diseases of the genitourinary system.

28 Intestinal infectious diseases are defined by ICD-10 codes A00 to A09, excluding A02.1 (salmonella septicaemia) which was included in the definition of sepsis.

29 Viral infections involving skin lesions correspond to the ICD-10 category "Viral infections characterized by skin and mucous membrane lesions", B00 to B09.

30 Joinpoint Regression Program, Version 4.0.4 – May 2013. Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute.

**Appendix A**

**Opioid-associated mortality, by selected underlying cause of death, Canada, 2000 to 2011**

| Underlying cause of death | Opioids recorded as underlying cause of death | Opioids recorded as contributing cause of death | Opioid-associated mortality |
|---|---|---|---|
| | number of deaths | | % of all deaths |
| Diseases of the skin and tissue | 0 | 736 | 61.9 |
| Infectious and parasitic diseases | 4824 | 7245 | 53.4 |
| Diseases of the digestive system | 0 | 5279 | 16.3 |
| Diseases of the urinary system and genital organs | 0 | 2545 | 16.0 |
| Diseases of the muscles, skeletal system and connective tissue | 0 | 736 | 15.9 |
| Conditions originating during the period immediately before and after birth | 125 | 125 | 7.9 |
| Diseases of the respiratory system | 0 | 3045 | 5.9 |
| Endocrine, nutritional and metabolic diseases (e.g. diabetes, metabolic syndromes) | 0 | 1775 | 5.0 |
| Congenital disorder of the embryo or fetus (congenital anomalies) | 0 | 705 | 4.8 |
| Mental and behavioural disorders | 0 | 7245 | 4.0 |
| Diseases of the nervous system | 0 | 1375 | 3.7 |
| Cancer | 0 | 7140 | 3.2 |
| Diseases of the circulatory system | 0 | 8855 | 2.3 |
| External causes (e.g. accidents, homicide, suicide) | 0 | 965 | 1.8 |
| All causes of death | 7536 | 62310 | 5.5 |

**Note:** The counts in this table have been rounded to the neighbouring multiple of 5 to meet the confidentiality requirements of the Statistics Act.

**Source:** Statistics Canada, Vital Statistics – Death Database